THE MECHANISM OF ELIMINATION OF BACTERIA FROM THE RESPIRATORY TRACT.

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As long ago as 1868, Lister[1] noted that penetration of the lung by a fractured rib did not lead to infection of the pleural cavity even though the latter was brought in contact with the outer world by means of the inspired air. This observation was eventually followed by systematic studies which showed that in health the lungs are entirely or almost entirely bacteria-free, and a similar state of affairs was found to exist in the deeper nasal passages. The means whereby this condition of relative sterility is maintained has been carefully worked out, but the possibility of a similar protective mechanism in the mouth does not seem to have been entertained by those interested in the contiguous portions of the air passages. On the contrary, it has been generally assumed that the buccal cavity may be likened to an open Petri plate filled with a medium favorable for any entering bacteria, and superficial support for this idea comes from the actual identification of numerous varieties of organisms both saprophytic and pathogenic in cultures made from the mouth.

In the course of experiments made in the past three years we have been able to show that despite the presence of a profuse indigenous flora the mouth is as adequately protected against the colonization of foreign bacteria as are the lungs or deeper nasal passages. It is the present purpose, therefore, to review what information is at hand about the whole question of the protective mechanism of the upper air passages and to indicate its significance in relation to the spread of infectious disease. One may consider in the case of each of the various regions (mouth, nasal passages and lungs) the following factors of possible importance: (*a*) anatomic conditions; (*b*) the flushing mechanism; (*c*) bactericidal action of secretions; (*d*) reaction of secretions; (*e*) the antagonistic action toward invaders of the indigenous flora, and (*f*) phagocytosis.

The Protective Mechanism of the Mouth. As will be seen later, the presence of bacteria is avoided in the case of the nose and lungs largely by anatomic conditions which prevent the entry of organisms into these regions. It is of interest that the anatomic structure of the mouth does not in itself seem designed to prevent invasion. Inasmuch as the function of the mouth, as entrance to the alimentary canal, makes it impossible to avoid the constant introduction of bacteria, a mechanism has been developed which acts by elimination rather than by filtration. But before discussing the details of this mechanism we may outline briefly the demand made upon it as well as what is actually accomplished by it. A host of foreign organisms is continually entering the buccal cavity. Of these the largest element is that carried in with food and drink. Milk, for example, usually contains many organisms, and various kinds of food, such as cheese, are swarming with bacteria and moulds. Fingers, cigarettes, stamps, and in the case of children, foreign objects of all sorts with bacterial content varying in kind and in extent, also make their way into the mouth, and finally a smaller number of organisms is constantly being inhaled. But if repeated throat cultures are made in normal people one finds not the diverse and variable flora which would be expected but a relatively simple and constant one. Revealed by aërobic methods there are a few predominating groups: The non-hemolytic streptococci, the Gram-negative cocci, diphtheroids and staphylococci—none of them organisms which are abundantly present in food or in the air. In addition one may find a miscellaneous group of transient bacteria which are present only for brief periods of time and are clearly intercepted by the culture swab in their passage through the mouth. Foreign pathogenic organisms are rarely found over long periods of time save when associated with a local focus of infection. In summary then there is evidently a rapid and effective elimination of the horde of incoming organisms whereby they are segregated from the normal indigenous flora.

An analysis of this process of elimination indicates that it is accomplished mainly by a system of flushing which operates in two ways: In the first place the gross act of swallowing propels the major portion of ingested material by forcible contractions of the muscular masses of tongue and pharynx directly into the esophagus. If a suspension of charcoal or a solution of a dye is swallowed there is intense staining of the dorsum of the tongue, of the palate and of the cheeks, but little or none of the sublingual space, tonsils or upper pharynx.[2] Furthermore, if a suspension of bacteria containing many million organisms per cubic centimeter is ingested and cultures are then made from various sites in the mouth and throat, relatively few colonies are recovered, and these are confined largely to the tongue.[3] In one such experiment nine colonies of the organism introduced grew in the culture from the pharynx and less than fifty were obtained from the tonsils. The swallowing mechanism operates therefore toward a rapid and direct removal of material without any churning action or tendency toward unnecessary contamination of the whole mouth cavity and without forcible implantation of many bacteria upon the mucous membranes.

In association with the above crude system of flushing a more highly organized mode of elimination may be demonstrated. If foreign particles or bacteria are implanted directly on the mucous membranes of the tongue, tonsil or pharynx it is found that they can no longer be readily dislodged. They adhere firmly in the tenacious mucus and are not removed by such procedures as rinsing or gargling. But once fastened in this way the particle or organism is drawn rapidly backward by a series of suction currents and is swallowed. The paths of these currents are quite direct. Bacteria implanted on the right side of the tongue, for example, travel backward on this side without crossing the midline and without contaminating the tonsil unless the latter is prominent; from the tonsil or pharynx they always move toward the esophagus —never forward into the mouth.[2 3]

The net effect of the operation of this mechanism we have tested by experimentally introducing various bacteria into the mouths of men. The general result has been that within twenty-four hours such organisms as the colon bacillus, staphylococcus, influenza bacillus, streptococcus and Friedländer bacillus are entirely eliminated.[4] It would appear, therefore, that the chance foreign pathogen introduced by natural means would ordinarily have but little chance of colonizing.*

In this connection a word may be said about the function of the tonsils. As pointed out by various writers, for example, Crowe,[5] it is generally believed that the ring of lymphoid tissue in the pharynx acts as a barrier which protects the lower air passages by catching up bacteria which enter the mouth or nose. Many organisms undoubtedly do enter the tonsil crypts, but in view of the experiments reported above[2] it seems that such invasion occurs rather in spite of the mechanism which tends to spare the tonsils than as a beneficial event. Few would claim nowadays that the tonsils which have come to be regarded as notoriously injurious foci of infection serve any useful protective function.

While the flushing mechanism outlined above undoubtedly constitutes the major or first line of defence against colonization of bacteria in the buccal cavity, there are other factors to be considered. The bactericidal action of the saliva is certainly of some importance. While the literature on this subject is confusing and unsatisfactory,[6] as it deals only with test tube experiments which can hardly be applied to actual conditions in the mouth, it has been possible to show in the case of at least one variety of bacteria—sarcina lutea—that the saliva exerts a rapid actual destructive action *in vivo:* killing the organisms within fifteen minutes to one hour.[7] It may be that other organisms are similarly destroyed, but even in cases in which there is no true bactericidal action there may be an inhibitory or bacteriostatic effect. This is a complex question of great interest which requires much more study. It seems of particular importance because even a slight bacteriostatic effect may be adequate to inhibit the activity of a foreign organism until it can be eliminated by the flushing mechanism.

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* We use this term to indicate a biologic reaction between the organism and the host which allows the growth *in situ* of the former.

The reaction of the mouth secretions must be considered apart from their other qualities. Recent work has brought out the tremendous importance of hydrogen-ion concentration in the growth of bacteria and of tissues *in vitro,*[8] and the question is raised whether reaction is not influential in favoring or inhibiting growth *in vivo* as well. It is suggestive that the reaction of most salivas—p^{H} 6.0—p^{H} 7.3— is more acid than that which has been found to be the optimum for growth of pathogenic bacteria such as pneumococci, streptococci, and influenza bacilli in the test tube—namely p^{H} 7.4—p^{H} 7.6. In fact the p^{H} of the majority of human salivas is greater than that which allows initiation of pneumoccus growth at all in artificial media.[10] One may then safely conclude that the reaction of the mouth secretions does not favor most foreign bacteria; to what extent it actually has an inhibitory effect of practical importance cannot be definitely stated as yet.

Still another possible factor is that of antagonistic action against foreign bacteria by the normal mouth flora. Test-tube experiments seem of little value in settling this point and experimental approach is difficult, but occasional observations indicate that one organism may dislodge another. Patient F. yielded hemolytic influenza bacilli in large numbers on three successive cultures from the pharynx. Two days after the last examination he developed an acute tonsillitis. Thereafter on numerous cultures made over a period of two months hemolytic streptococci were present in almost pure culture, but hemolytic influenza bacilli were no longer found. Patient A. on first culture showed mixed throat flora. On the second and third cultures the plates were covered with Friedländer bacilli. There had been no clinical reaction. Two more cultures were made, using a system of dilutions so that only twenty-five to fifty colonies of Friedländer bacilli were present on each plate. Even with this dilution, which probably eliminated overgrowth on the plates, no other organisms were present, indicating that they were largely or entirely absent at the site of culture. It may be therefore that a balance of power among the various inhabitants of the mouth is an accessory factor in inhibiting the growth and colonization of foreign invaders.

Although the present discussion concerns itself with the means whereby colonization or establishment of growth on respiratory mucous membranes is prevented, for the sake of completeness one must mention the last line of defence, namely, the protective activities of the body fluids and cells. This point is brought up because there is evidence that even without production of disease occasional penetration of intact mucous membranes by bacteria may occur.[11] Whether in such cases at least a physiologic lack of continuity exists is a much-disputed academic question, which need not be discussed in the present connection. The point of importance is that even should a foreign organism escape elimination of the flushing mechanism—caught up, let us say, in a crevice of the mucous membrane—there still remain possible modes of effective disposal.

The Nasal Passages. While the protective mechanism of the mouth consists mainly of elimination, that of the nose operates especially by prevention of invasion; anatomic considerations are unimportant in the former, essential in the latter. Entry of bacteria into the nose follows almost always the inhalation of bacteria-laden dust or droplets; direct introduction, which is the usual event in the case of the mouth, rarely occurs. If one considers the structure of the nasal passages it is apparent that no direct open path exists in the line of the air currents but that such currents immediately impinge upon the turbinated bones. Furthermore, these are so constructed that the stream of air is not only broken up but is deflected in numerous directions. A satisfactory demonstration of this fact is obtained by study of frontal sections through the nasal passages at various levels. As a matter of fact, most of the inhaled bacteria are arrested (probably by the network of moist vibrissæ) very near the anterior nares, as shown by Hasslauer,[12] Thompson and Hewlett[13] and others, who found large numbers of organisms at the nasal orifices and few or none in the deeper air passages. But inasmuch as the nasal mucosa is covered with a film of mucus, any organisms which do penetrate are promptly caught up and rapidly swept by the current of the ciliated epithelium toward the pharynx and esophagus. Thompson and Hewlett noted the speed of the ciliary curret in the frog's pharynx to be as great as one inch per minute, and by actual experiment we have found that organisms placed in the nose may be recovered from the pharynx after as short a space of time as ten minutes. In summary, then, we have an effective self-cleaning filter which purifies the air of bacteria before it enters the lungs.

Whether or not other elements enter into the protective mechanism of the nasal passages is uncertain. Thompson and Hewlett obtained evidence that bacillus prodigiosus was destroyed in the nose, and conclude without justification that few or no bacteria introduced into the nares can reach the pharynx alive. There are also certain incomplete and dubious experiments on record as to the bactericidal action of the nasal secretions[14] *in vitro*. This part of the subject requires much further study before final statements can be made.

The Lungs. The question of how the lungs are guarded against infection is one of great interest, and in considering this matter our main point of approach must be the outstanding fact that in health few or no bacteria are present below the larynx. While direct evidence from human beings is not readily obtainable, cultures made from the lungs of healthy animals are almost uniformly sterile. The most significant observations on this point with which we are familiar are those of Heuer.[15] This observer, in the course of experimental excision of the lung in dogs, made numerous cultures from the bronchial stump. In no case were any organisms found. On the other hand it is known from postmortem appearances that dust and carbon and metal particles do reach the lung, and it seems very likely that some few bacteria are introduced as well. The history of this question is an interesting one and many observations are on record which seem contradictory. Paul,[16] Neuninger[17] and Quesnil[18] give a comprehensive review of the literature on the subject of the bacterial content of the normal lung and attempt to reconcile the diverse findings of various writers. When one considers that some studies were made a considerable length of time after death, some in cases in which there had been a long agonal period, and that in others the subjects were animals who burrow in fodder and inhale heavily bacteria-laden dust, it is clear that one can draw no final conclusion as to the usual state of affairs in man. It seems certain, however, that in health and under average conditions of dust exposure it is only the occasional organism which penetrates below the larynx. It appears then that the protective mechanism of the lung includes two main factors: (*a*) An anatomic structure which cuts off most of the organisms from the inspired air, and (*b*) a process which destroys or eliminates the few which do penetrate.

The anatomic element seems of greatest importance. As pointed out above the entering current of air, whether through nose or mouth, is deflected against complex mucous-covered surfaces which catch up bacteria and act as filters. In regard to the question of how many bacteria actually do pass these barriers the experiments of Paul[16] are of special significance. This observer placed rabbits in a glass chamber into which a suspension of bacillus prodigiosus was sprayed. After one-half hour of this treatment the animals were killed and cultures were made from the lungs under proper precautions. Prodigiosus was invariably found, sometimes as many as 500,000 colonies in part of one lung. By an ingenious calculation, Paul reached the conclusion that 4 per cent of the inspired organisms had reached the lung, and reasoned further that under spontaneous conditions a similar fraction of the inspired bacteria might penetrate. We are not convinced that this reasoning is correct—probably there is a proportionate decrease in the number of bacteria reaching the lung as the number in the air decreases, but none the less the fact remains that the filter is not a perfect one and that at times organisms do actually penetrate beyond the larynx. Paul also showed by a rather artificial experiment in which he introduced a foamy suspension of prodigiosus into the mouths of rabbits that droplets formed by the bursting of bubbles *in situ* might be inhaled, as indicated by subsequent recovery of the organisms from the lung. In actual life the bacterial content of the air is variable. In dusty rooms it may be as great as several hundred thousand per cubic meter, but this is unusual. The chances, therefore, of pathogenic bacteria reaching the lungs of normal people by direct inhalation are slight.

The main factor then in the protective mechanism of the lung is a highly effective but not infallible filter. What is the fate of the few organisms which do pass the larynx in health? Three possibilities must be considered. The bacteria may be removed, they may be destroyed in the lung or they may set up disease.

The trachea and larger bronchi are lined with ciliated epithelium which sweeps toward the larynx. We know that inhaled dust is carried up by this process and expectorated mixed with mucus; doubtless bacteria are eliminated in the same way. That this is not the only element involved in removing bacteria from the lung is indicated by an experiment such as the following: Paul sprayed rabbits with prodigiosus and found that after twenty-four hours only 1/35000 as many colonies were present in the lung as after the treatment, whereas in a similar experiment with subtilis spores 6/11 of the number originally inhaled could be recovered after twenty-four hours. This would suggest some other process besides a simple mechanical removal. Simultaneous cultures from lungs and bronchial nodes[18] indicate that many bacteria are removed by lymphatic drainage, and finally some organisms finding themselves in unfavorable surroundings may die *in situ* in the lung.

In summary, then, in health a very effective protective mechanism exists which operates against the colonization of bacteria in the lung. The main element is a filtration system which allows only few organisms to enter. These, unless they produce disease, are eliminated by the ciliary current, by dying *in situ* or by being carried off through the lymphatics.

Above we have sketched briefly the *modus operandi* of the protective mechanism against the colonization of bacteria in the respiratory tract, recognizing that our knowledge is still in the most rudimentary stage. The essential point, however, seems to be a system of mechanical filtration and flushing aided by influences which temporarily arrest the aggressiveness* of foreign organisms (reaction and bacteriostatic effect of saliva, antagonistic action of mouth bacteria) until they can be removed.

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* This term is not used here in the technical sense.

So far we have stated the case altogether in favor of the host and against the invader. But experience shows that the protective mechanism, while theoretically adequate, often breaks down in actual fact with consequent colonization of foreign bacteria and production of disease. It seems pertinent, therefore, to examine the matter from the other side and to analyze the factors which lead to failure of the protective mechanism.

1. *Dosage.* There exist certain bacteria of such virulence that a single cell may suffice to infect a susceptible animal. On the other hand we find organisms of such a nature that no number however great seems capable of setting up disease. In the vast majority of cases, however, it is dosage which is the determining factor in experimental infection. Numerous observations indicate its importance in human disease also. We may perhaps think of infection in terms of a balance struck between the race and various types of bacterial invaders which tends to keep up an average incidence of infectious diseases among large groups of people. But in the individual case an overwhelming dose of organisms may regularly produce disease. It seems altogether reasonable to suppose that the protective mechanism of the respiratory passages, unless it were perfect, in its action would be more effective against a smaller than against a larger dose of foreign pathogens. While single organisms successively introduced might be disposed of thousands of times before a weak point in the defence could be taken advantage of, some one or another of a thousand organisms simultaneously introduced might find favorable conditions for colonization or invasion even though all the rest of the group were eliminated. It is likely therefore that, other things being equal, dosage is of importance in explaining certain instances of breakdown of the protective mechanism.

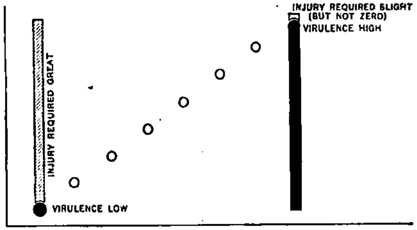
2. *Anatomical Features.* In the experiments which were made on the fate of charcoal particles introduced into the mouth it was noted that anatomical variations frequently led to a disturbance of the normal currents of removal. In one instance it was possible to watch for several hours a small mass of carbon particles which had been arrested above a bit of protruding lymphoid tissue on the posterior pharyngeal wall. Furthermore, particles and bacteria must be frequently caught up in the tonsillar crevices despite their relatively protected position. It may well be then that an organism which would be harmless if promptly eliminated may be enabled to unfold pathologic activity if arrested in the throat for any length of time.

3. *Lag.* An old observation in bacteriology is to the effect that a single organism inoculated into a flask of broth may fail to grow, whereas a larger inoculation may result in profuse develop-

ment. Further study of this phenomenon has shown that the various members of a culture are not equally viable at all ages and that senescence sets in early. If such senescent organisms are transferred to a fresh medium a latent period exists before active growth is again resumed by the culture as a whole. This phenomenon of lag has been carefully studied by Chesney,[19] who has worked out its laws especially in the case of pneumococcus. But pathogenic organisms as they enter the body from certain outside sources are probably not always in an active vegetative state. When dried in dust or on objects they usually assume an inactive or resting form. It is fair to conclude, therefore, that many pathogenic organisms as they enter the respiratory passages are in a state of greater or less inhibition. Such inhibition may be important in allowing their removal before activity is resumed. Conversely, if the organism enters the mouth while in an actively vegetative state its chances of colonization should be greater. Such a condition of affairs would apply especially to organisms transferred directly by cough through the air from one individual to another. It is of interest that in epidemics of acute infections such as those which occurred in the army camps one was dealing with a concentration of individuals and hence with a rapid transmission of organisms by very direct routes, indicating that a highly vegetative state of the bacteria existed.

4. *Injuries.* Perhaps the most important factor leading to a breakdown of the protective mechanism is some type of injury. Before taking up this point, however, a few words must be said about virulence and resistance.

Virulence. As a rule this term has been loosely used to indicate that the organism in question is producing a more or less severe and highly contagious form of disease. More exact definition is however necessary; in other words, does a highly virulent organism possess intrinsically any greater invasive power than a less virulent member of the same species, and if the two were deposited on a perfectly intact and healthy mucous membrane would the one be able to invade and produce disease while the other could not? It seems that definite evidence of any such difference is lacking, but that in the case of the virulent organism a much slighter injury or defect and perhaps an injury or defect of a different sort is adequate to allow invasion. In the case of an extremely virulent organism one can picture the requisite injury being so slight as to approach zero. The point may best be brought out by a specific example such as streptococcus infection. Under ordinary conditions the streptococcus is clearly a secondary invader. Its role in terminal infections, in scarlet fever, in measles and in influenza may be mentioned. Here it unfolds its activities on tissue damaged by an independent primary process. During the war, following the rapid and extensive passage of streptococci through large numbers of patients with measles, strains appeared which finally on superficial scrutiny seemed able to produce primary disease. It seems much more likely, however, that these exalted strains were simply able to take advantage of a minute lesion, perhaps a minute mechanical injury of the mucous membranes, which under ordinary circumstances would not suffice to allow the entry of an organism of average virulence. This idea is supported by the clinical observations of every type of transition between the streptococcus as an obvious secondary invader, and the streptococcus as an apparent primary invader. The situation may be diagrammed as follows:



In further support of this idea the following facts may be mentioned: (*a*) The usual prompt elimination of foreign organisms naturally or experimentally introduced into the upper air passages; (*b*) the corroborative evidence of the rarity of the production of certain diseases by direct contact such as lobar penumonia; and (*c*) the fact that the incidence of a disease due to a highly "virulent" organism may be lower than that of a disease due to a less "virulent" one. For example, the incidence among pneumonia cases of type III infection is only about 10 per cent with a mortality rate of 50 per cent, whereas type I infections, which make up 25 to 30 per cent, of the whole, have a mortality of only 20 to 35 per cent.[20] Furthermore, the type III organism is more widely distributed among the population in general than type I. Clearly the invasive power of these organisms does not run parallel with the severity of the infection produced by them.

In summary, then, while the virulence of an organism may establish the mortality rate among those infected, and may to some extent determine the incidence of infection in so far as the highly virulent organism may take advantage of a slight injury to the host so that it can invade, in the last analysis the production of disease seems to be made possible by an injury or defect which is more or less independent of the organism. This generalization seems to apply to the common respiratory pathogens such as pneumococcus, streptococcus, meningococcus, and the influenza bacillus. Whether other viruses such as the hypothetical ones of the acute exanthemata can produce their own injury requisite for invasion is still uncertain.

Types of Injury Important in the Production of Respiratory Infection. Such injuries may be mechanical, thermal, chemical or infectious.

A. *Mechanical Injuries.* Purely mechanical injuries probably play only a minor part in facilitating infection. The mucous membranes, however, undoubtedly suffer constant slight traumata which may create portals of entry for highly virulent organisms. Such lesions may well account for many sepses of so-called cryptogenetic origin. They also undoubtedly play a part in the production of erysipelas. We have observed three cases of septicemia directly following the mechanical cleansing of tonsil crypts during the course of acute tonsillitis. Blake[21] was unable to produce pneumonia in monkeys by placing virulent cultures of pneumococci in the throat, but after injuring the trachea with a needle puncture invasion became possible. It is well established that postoperative lung abscess is due to the forcible inhalation of bacteria-laden bits of blood clot, following the elimination of the protective reflexes by the anesthetic. Disturbances of the cilia-bearing epithelium of the nose by operative measures often leads to subsequent chronic inflammation with colonization of bacteria. Finally, as an instance of mechanical disturbance of the bacteria eliminative mechanism, an observation made by us in a patient with bulbar palsy may be recorded. In this case sarcina lutea placed on the tongue was not removed by the usual suction currents but remained confined to the site of inoculation during the whole period of the experiment.

B. *Thermal Injuries.* The question of the relation of cold to respiratory infection is of interest. The recent thorough experiments of Mudd[22] and his associates indicate that thermal variations lead to marked vasomotor and secretory changes in the upper air passages. These writers bring a certain amount of evidence[23] that the bacterial flora may be modified following such reactions and give an important lead for further study.

C. *Chemical Injuries.* Chemical injuries may undoubtedly produce lesions which disturb the normal eliminative mechanism and allow bacterial invasion. Two promient examples may be quoted: War-gas poisoning,[24] if of any degree of severity, is followed by bronchopneumonias and histologic studies of the tissues show the bacteria actually invading the mucous surfaces denuded of their protecting epithelium. Poisoning with certain arsenicals allied to arsphenamine is accompanied by a severe erythema of the respiratory mucosa. This is soon followed by a bronchopneumonia clearly secondary to the chemical injury. We have observed three instances of this condition.

D. *Infection.* In this group falls perhaps the most important kind of injury which leads to secondary bacterial invasion in the upper respiratory tract. The role of measles, scarlet fever, influenza, smallpox and the exanthemata in general in allowing secondary infection is notable. In these diseases the "erythema" of the respiratory mucosa is associated with a disturbance of the normal protective mechanism following which secondary infections with various organisms readily occur. Olitzky and Gates[25] bring experimental support for this idea in the case of influenza. The common cold frequently draws in its wake a series of obvious minor secondary infections, and perhaps just as often serves as the predisposing factor for more serious infections. A careful clinical study of such diseases as lobar pneumonia and meningitis might disclose such preliminary injuries.

5. *Adaptation.* However much one may try to reduce the protective mechanism to a concrete basis there still remains a factor to be considered, namely, inherent adaptation of certain bacteria to growth on human mucous membranes. In another place we have presented evidence that some bacteria not members of the normal flora which are potentially capable of producing disease may become more or less completely adapted to free growth on normal mucous membranes.[26] This is true of influenza bacilli, green-producing streptococci and probably many other bacteria. Under such conditions the organism is not eliminated but is at hand over long periods of time. Then if proper accessory conditions arise invasion and disease may follow.

Discussion. The problem of infection may be approached from either of two standpoints—that of infection in groups of people or that of infection in the individual. Under the former head there are to be considered the broad general questions of the spread and incidence of disease—the nature and course of epidemics, the seasonal occurrence of various diseases, and their geographical distribution. A great stock of information in regard to these matters has been accumulated through the recording of gross facts and to a lesser extent by experimental studies of epidemics in animals, but the final determination of the laws governing infection has not yet been achieved. Contradictions constantly come up. In the case of a pandemic of influenza, for example, it seems established from the general sequence of events that we are dealing with a disease due to a living virus and one which is highly contagious. But when one attempts to explain the details of its spread, insurmountable difficulties immediately arise. The high incidence of the disease in certain localities among special groups of people with the sparing of others, the sparing of particular individuals for a considerable length of time (despite constant exposure) with ultimate infection, and the question of the sporadic case may be mentioned as examples of the difficulties which present themselves. Again, in the case of lobar pneumonia, despite the evidence in favor of transmission by carriers or dust, these general principles seem inadequate in working out the origin of individual infections.

Aside from such broad considerations we have to deal with the problem of infection in the individual, and here a different approach must be used. The general facts of epidemiology tell the number of people in a community likely to be affected by a certain disease under given conditions, a solution of the problem of infection in the individual will tell why A. is affected rather than B. and C. rather than D.

In an attempt to clarify this latter phase of infection with reference to respiratory disease the above analysis is presented. It has seemed profitable to avoid, as far as possible, such vague terms as virulence and resistance and to reduce the facts to concrete terms. The most general conclusion is to the effect that there exists in the respiratory passages—nose, throat, mouth and lungs—a mechanism which tends to eliminate foreign particles and bacteria.

It is also clear that this eliminative mechanism has many imperfections and that in actual practice it often breaks down; it should be thought of rather as a tendency than as a rigidly efficient process, as relative and not as absolute, differing with different organisms and with a host of secondary conditions.

Again, it seems unwise to go too far in assigning purposeful protective qualities to the eliminative mechanism, and we wish merely to stress and to classify facts which may be helpful in explaining the means whereby colonization of bacteria is prevented or favored. A word of speculation may however be allowable. The classical viewpoint in regard to recovery from infection, or protection against infection, based on theories of humoral immunity, assumes a positively destructive action in disposing of foreign bacteria. It is now becoming more and more evident that the simple absence of favorable circumstances for the organism may be just as effective as any positively destructive action. Test-tube experiments are very clear on this point. Pneumococci, for example, when growth is once started may multiply in broth until a limiting reaction of p^H 5 is reached. Growth cannot, however, be initiated below p^H 7 in the same medium. In studying the action of dyes on bacteria it has also been shown that inhibitory or bacteriostatic effects are perhaps of as much importance as actual bactericidal action. It seems that this principle should be extended to human infection and that the respiratory protective mechanism is perhaps largely a matter of absence of favorable conditions for the foreign organism rather than any positively destructive process, although such action may be shown in certain instances. The main point, then, which we wish to make is the following. It has usually been assumed that the presumption was in favor of the invading organism and that the body was obliged to call forth special protective process to prevent infection. Now it is clear that the microörganism is, on the whole, at a disadvantage and that no special response is, as a rule, required to dispose of it, but that special favoring circumstances for the organism must be present before infection can take place.

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TWO HUNDRED SYPHILITIC PATIENTS WHOSE CHIEF COMPLAINT WAS "STOMACH TROUBLE;" AN INTERPRETATIVE ANALYSIS OF THE DIAGNOSIS OF SYPHILIS IN CONSULTANT MEDICAL PRACTICE.

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